

CLAIMS

1. An isolated nucleic acid encoding a mammalian TRAIL receptor selected from the group consisting of DR5 and TRAIL-R3, splice variant cDNA sequences thereof, or an active fragment thereof.

2. The nucleic acid according to claim 1, wherein said mammalian TRAIL receptor is isolated from a mammal selected from the group consisting of human, rat, mouse, porcine, ovine, canine and bovine.

3. The nucleic acid according to claim 1 wherein the encoded splice variant is DR5s, or an active fragment thereof.

4. The nucleic acid of claim 3 comprising SEQ ID NO:5 or an active fragment thereof.

5. A nucleic acid encoding a mammalian TRAIL receptor, wherein said nucleic acid is selected from the group consisting of:

(a) DNA encoding the amino acid sequence set forth in SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6;

(b) DNA that hybridizes to the DNA of (a) under moderately stringent conditions, wherein said DNA encodes biologically active DR5 or TRAIL-R3;

(c) DNA degenerate with respect to either (a) or (b) above, wherein said DNA encodes biologically active DR5, or TRAIL-R3; and

(d) splice variant cDNA sequences of any of (a) - (d).

6. The nucleic acid according to claim 5 wherein the splice variant cDNA comprises SEQ ID NO:5.

7. The nucleic acid according to claim 5, wherein said nucleic acid hybridizes under high stringency conditions to SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

8. The nucleic acid according to claim 5, wherein the nucleotide sequence of said nucleic acid is substantially the same as nucleotides set forth in SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

9. A nucleic acid according to claim 5, wherein the nucleotide sequence of said nucleic acid is SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

10. A nucleic acid according to claim 5, wherein said nucleic acid is cDNA.

11. A vector containing the nucleic acid of claim 5.

12. An expression vector comprising the nucleic acid of claim 5, wherein the nucleic acid encoding the TRAIL receptor is operatively linked to a promoter.

13. Recombinant cells containing the nucleic acid of claim 5.

14. An antisense oligonucleotide capable of specifically binding to mRNA encoded by said nucleic acid according to claim 5.

15. An isolated mammalian protein selected from the group consisting of DR5, a DR5 splice variant, TRAIL-R3, and a TRAIL-R3 splice variant, wherein said protein is characterized by being able to bind TRAIL ligand.

16. The protein according to claim 15, wherein the amino acid sequence of said protein comprises substantially the same sequence as the protein sequence set forth in SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

17. The protein according to claim 16, comprising the sequence set forth in SEQ ID NO:2, SEQ ID NO:4, or SEQ ID NO:6.

18. The protein according to claim 15, wherein said protein is encoded by a nucleotide sequence that is substantially the same as SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

19. The protein according to claim 18, wherein said protein is encoded by a nucleotide sequence set forth as SEQ ID NO:1, SEQ ID NO:3, or SEQ ID NO:5.

20. A method for expression of a protein selected from the group consisting of DR5, a DR5 splice variant, TRAIL-R3, and a TRAIL-R3 splice variant, said method comprising culturing cells of claim 13 under conditions suitable for expression of said protein.

21. An isolated anti-DR5 or anti-TRAIL-R3 antibody having specific reactivity with a protein according to claim 15.

22. The antibody according to claim 21, wherein said antibody is a monoclonal antibody.

23. The antibody according to claim 21, wherein said antibody is a polyclonal antibody.

24. A composition comprising an amount of the antisense oligonucleotide according to claim 14 effective to inhibit expression of a human DR5 or TRAIL-R3 protein and an acceptable hydrophobic carrier capable of passing through a cell membrane.

25. A transgenic non-human mammal expressing exogenous nucleic acid encoding a DR5 or TRAIL-R3 protein according to claim 15.

26. A transgenic non-human mammal according to claim 25, wherein the transgenic non-human mammal is a mouse.

27. A method for detecting the presence of a mammalian DR5 or TRAIL-R3 protein in a sample, said method comprising contacting a test sample with an antibody according to claim 21, detecting the presence of an antibody-DR5 complex or antibody-TRAIL-R3 complex, and therefrom detecting the presence of a mammalian DR5 or TRAIL-R3 protein in said test sample.

28. A bioassay for evaluating whether test compounds are capable of acting as agonists or antagonists for DR5 or TRAIL-R3 proteins according to claim 15, said bioassay comprising:

(a) culturing cells containing: DNA which expresses DR5 or TRAIL-R3 proteins or functional modified forms thereof, wherein said culturing is carried out in the presence of at least one compound whose ability to modulate apoptotic activity of DR5 or TRAIL-R3 protein is sought to be determined, and thereafter

(b) monitoring said cells for either an increase or decrease in the level of apoptosis.

29. A bioassay for evaluating whether test compounds are capable of acting as antagonists for DR5 or TRAIL-R3 proteins according to claim 18, or functional modified forms of said DR5 or TRAIL-R3 proteins, said bioassay comprising:

(a) culturing cells containing: DNA which expresses DR5 or TRAIL-R3 proteins, or functional modified forms thereof, wherein said culturing is carried out in the presence of: increasing concentrations of at least one compound whose ability to inhibit apoptotic activity of DR5 or TRAIL-R3 proteins is sought to be determined, and a fixed concentration of TRAIL; and thereafter

(b) monitoring in said cells the level of apoptosis as a function of the concentration of said compound, thereby indicating the ability of said compound to inhibit DR5 or TRAIL-R3 apoptotic activity.

30. A method for modulating the apoptotic activity mediated by DR5 or TRAIL-R3 protein, said method comprising: contacting said DR5 or TRAIL-R3 protein with an effective, modulating amount of said agonist or antagonist identified by claim 28.